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Two case studies assessing the effect of oral contraceptive pills upon serum AMH concentrations: Results from an external quality assurance (EQA) scheme

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ABSTRACT

Objective: To describe the effect of combined oral contraceptives (COC) on serum AMH level in 2 women. **Methods:**The COC was initially stopped after over 12 years use then restarted, with the serum being analysed by 6-8 laboratories in an EQA scheme using the same assay (Beckman Coulter Gen II). **Results:**In both women, the AMH rose significantly after cessation of the pill, and then dropped after resumption. **Conclusions:**In summary, AMH was affected by the combined oral contraceptive pill and further studies on the effect of oral contraceptives are warranted.

1. Introduction

Anti-müllerian hormone (AMH) has been shown to be a useful marker of ovarian reserve [1]. With its increasing clinical utility, attention has been paid to different clinical situations that might affect the AMH levels and hence their interpretation. The use of oral contraceptives was of interest given the suppression of ovarian follicular development and ovulation seen with often different forms of the pill [2]. AMH concentrations were not thought to be modified by the use of oral contraceptives [3, 4] allowing ovarian reserve to be assessed whilst women were still on the pill, but this is not universally held as other reports have shown oral contraceptives to have a suppressive action [5-8]. The present report describes the experience of an external quality assurance scheme for AMH in which samples were analysed by a number of laboratories, showing longitudinal changes in two women stopping and then resuming oral contraception.

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2. Materials and methods

2.1. Blood collection

Blood samples were collected by venepuncture and separated immediately by centrifugation. The serum was allowed to clot at room temperature for 1 hour and the clot removed. Serum was decanted and stored at 4 ℃ prior to packing, and distributed within 3 days to laboratories participating in the External Quality Assurance Schemes for Reproductive Medicine (EQASRM; Northlands Western Australia 6905). All laboratories used the same assay kit, namely the Beckman Coulter Gen II ELISA (Beckman Coulter Australia Pty Ltd, Gladesville NSW 2111, Australia). Values were compared according to published reference ranges [9-11]. AMH concentrations for each woman were analysed initially by ANOVA using the StatistiXL add-in for Excel (StatistiXL, Nedlands, Western Australia 6009), followed by Tukey's HSD test, and differences considered significant if $P<0.05$.

2.2. Subjects

The first case was a 26 year old female, non-smoking, volunteer in good health, with no previous pregnancies, having a normal BMI, without any history of polycystic ovarian disease, and no family history of premature ovarian

failure or infertility. She had regular menstrual cycles before starting oral contraception, having commenced Micryogynon 30 (Ethinylestradiol, Levonorgestrel; Bayer Schering Pharma, Pymble NSW 2073, Australia) 12 years earlier for contraceptive purposes.

Case 2 was a 41 year old female volunteer with no previous pregnancies, a non-smoker with normal body mass index. However, she had previously been diagnosed with polycystic ovarian disease, with elevated androgens and oligomenorrhea, for which she had been taking Diane-35 (Ethinylestradiol, Cyproterone acetate; Bayer Schering Pharma, Pymble NSW 2073, Australia) for 14 years.

3. Results

Blood was taken when they had been off the pill for 1 month and 3 months, and then 3 months after resuming the pill. Serum samples were sent to 6-8 laboratories in each distribution, and all laboratories used the Beckman Coulter Gen II ELISA.

The AMH concentrations for the two women when on and off the pill are shown in Table 1. There were significant differences overall for each woman. Both women had levels consistent with reduced ovarian reserve after being on the pill for 12 years or more. Subsequent post hoc analysis showed that there were increases in the concentration once coming off the pill, becoming significant after 3 months. Once resuming the pill, AMH had returned to levels similar to the baseline values after 3 months.

Table 1

Serum AMH concentrations (mean ± sem) for two women on the pill for 12 or more years.

Medication	Time on or off medication	AMH concentration (pmol/L)	
		Case 1[a]	Case 2[b]
Pill	⩾12 years	7.8 ± 0.6	6.6 ± 0.8
None	1 month	11.6 ± 1.0	3.8 ± 0.3
	3 months	23.2 ± 1.5*	17.4 ± 2.0*
Pill	3 months	11.7 ± 0.9	3.9 ± 0.3

Data were expressed as Mean±SEM. [a]Micryogynon 30 ; [b]Diane-35,*P<0.001 vs the baseline figure on the pill.

4. Discussion

Many women in their reproductive years use oral contraception, and two main reasons for the measurement of AMH to measure functional ovarian reserve in such women have been proposed. Firstly, prolonged use of the contraceptives can suppress pituitary gonadotrophins and antral follicle development thereby creating an experimental opportunity to evaluate AMH as a marker of ovarian reserve rather than follicular growth[12]. Secondly, a clinical test in users of hormonal contraceptives for the differential diagnosis of anovulatory disorders and early menopause would be useful, and AMH would be an ideal candidate if it was found to be unaffected by oral contraceptives[13]. The effect of oral contraceptives on AMH in a number of clinical settings is unclear from the literature. Women with polycystic ovarian syndrome show either no change in AMH level after hormonal contraception[14] or a reduction[5], as do normally cycling women with no change[4, 12, 13, 15] or a reduction[7, 8, 16]. The present report has shown two case studies chosen at random that both demonstrate an increase in AMH when coming off the oral contraception followed by a reduction when the contraception was resumed. Further studies examining the effect of different pharmaceutical preparations in women of varying ovarian reserve would seem warranted.

Conflict of interest statement

We declare that we have no conflict of interest.

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